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10/006,911	11/08/2001	William Gaarde	RTS-0200	1396

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EXAMINER

SCHULTZ, JAMES

ART UNIT PAPER NUMBER

1635

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/006,911

Applicant(s)

GAARDE ET AL.

Examiner

J. D. Schultz, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 08 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,2,4-10 and 12-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-10 and 12-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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## **DETAILED ACTION**

### ***Status of Application/Amendment/Claims***

Applicant's response filed 8 September 2004 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 2 June 2004 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-10, and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Part of this rejection is drawn to a new matter issue as discussed below.

The invention of the above claims is drawn to modified compounds 8 to 50 nucleobases in length targeted to nucleobases 1345 through 2976 of human collapsin response mediator protein 2 of SEQ ID NO: 3, wherein said modified compound

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hybridizes with and inhibits the expression of human collapsin response mediator protein

2. The invention is also drawn to internucleoside linkages, nucleobase, and sugar modifications, chimeras, and methods of using said modified compounds.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, and any combination thereof.

To be clear, the claims submitted June 4, 2004 are considered to lack adequate support for the introduction of the term "modified compound" in claim 1, and thus this term is considered to constitute new matter. Furthermore, applicants are not considered to have adequately supported claims to the genus of any modified compound that inhibits human collapsin response mediator protein 2 of SEQ ID NO: 3 as recited in claim 1. The discussion for why these elements are considered to lack adequate description is considered in order below.

The specification is considered to lack adequate description for the genus of all modified compounds that target human collapsin response mediator protein 2 of SEQ ID

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NO: 3 as recited in claim 1, because applicants have not provided a definition of the term “modified”, which is therefore given its plain meaning which is considered very broad, encompassing significantly more than the molecules disclosed.

Applicants have not disclosed a sufficient number of structures that represent a full description of the breadth of this genus. Applicants have disclosed a number of antisense sequences that target and are perfectly complementary to SEQ ID NO: 3. Applicants have also disclosed a list of possible nucleotide modifications that would fall within the scope of the term “modified”. However, the term “modified” is considered to be much broader than mere nucleotide modifications. The term “modified”, according to The American Heritage Dictionary of the English Language, (Fourth Edition Copyright © 2000 by Houghton Mifflin Company. Published by Houghton Mifflin Company.) means “To change in form or character; alter.” Thus, the term “modified” is considered to add the “limitation” of alteration to the oligo without boundary, including not only structural modifications to each individual nucleotide, such as replacing any individual atom with another, but also changes to the sequence, among other things. Even taken conservatively, such language is considered to embrace virtually any sequence and compound so long as nucleobases are located somewhere within the molecule, including aptamers, PNA's, siRNA's, ribozymes, triplex forming oligos, nucleic acid/peptide conjugates, etc. Applicants simply are not considered to have adequately described a representative sample from such a genus of any possible modifications to oligos that target human collapsin response mediator protein 2 as claimed instantly. One of skill could not envision the species contained within such a broad genus of modified compounds containing nucleobases, particularly based upon a specification which merely

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teaches antisense oligonucleotides that are perfectly complementary to their target.

Applicants are not considered to have disclosed such breadth, and therefore the claims are rejected as containing new matter.

***Claim Rejections - 35 USC § 102***

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 12, 14 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Aguera et al. (U.S. Patent Application Number US 2002/0119944 A2, of record).

The claims of the instant invention are drawn to antisense compounds that target nucleobases 1345 through 2976 of SEQ ID NO: 3, which correspond to the coding region of SEQ ID NO: 3, or said compounds comprising internucleoside (i.e. phosphorothioate), sugar (i.e. 2'-O-methoxyethyl), nucleobase (i.e. 5-methylcytosine) or chimeras, or compositions comprising said compounds and pharmaceutically acceptable diluents or colloidal dispersion systems thereof, and methods of use.

Aguera et al. teach antisense compounds that target Ulip2 which corresponds to nucleobases 1345 through 2976 of SEQ ID NO: 3, and compositions comprising said compounds and pharmaceutically acceptable diluents, and methods of use.

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***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4-10, and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aguera et al. (U.S. Patent Application Number US 2002/0119944 A2) as applied to claims 1, 2, 12, 14 and 15 above, and further in view of Zhou et al., (GenBank Accession number U97105), Taylor et al. (Drug Disc. Today. 1999, 4(12) 562-567), Baracchini et al. (U.S. Patent Number 5,801,154), and Bennett (U. S. Patent Number 5,998,148). All but Bennett are of record.

The invention of the above claims is drawn to antisense compounds that target nucleobases 1345 through 2976 of SEQ ID NO: 3, which corresponds to the coding region of SEQ ID NO: 3, or said compounds comprising internucleoside (i.e. phosphorothioate), sugar (i.e. 2'-O-methoxyethyl), nucleobase (i.e. 5-methylcytosine) or chimeras, or compositions comprising said compounds and pharmaceutically acceptable diluents or colloidal dispersion systems thereof, and methods of use.

Aguera et al. teach antisense inhibition of Ulip-2 recorded at GenBank accession number U17279, which is identical to the coding portion of applicants' instant human collapsin response mediator protein 2 of SEQ ID NO: 3. Aguera et al. do not teach compounds that comprise internucleoside, sugar, nucleobase, chimeras, and 2' modifications, or compositions comprising said compounds and pharmaceutically acceptable diluents thereof.



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Zhou et al. teaches the full-length cDNA encoding human collapsin response mediator protein 2 of SEQ ID NO: 3.

Taylor et al. teach that antisense oligonucleotides 7-30 nucleotides long can be synthesized to inhibit the expression of any protein provided the cDNA sequence is known. Taylor *et al.* also indicate that making and using such oligos are available to those of ordinary skill in the art, that it is common practice to chemically modify the such oligonucleotides to prolong their bioactivity, and also teach that with software analysis and high affinity oligos, one needs to screen only 3-6 oligos to find one that inhibits its target 66-95% (p. 565).

Baracchini *et al.* teach that antisense oligonucleotides are preferably targeted to the coding region as instantly claimed, and also teach that preferred antisense oligonucleotides are modified in their sugar, backbone linkage and nucleobase composition (col. 6). Baracchini teaches that such modifications are desirable in antisense oligos because these modifications have desirable properties such as enhanced cellular uptake, enhanced affinity for nucleic acid targets and increased stability in the presence of nucleases. Baracchini et al provide specific embodiments of such modifications at columns 6-8 and in Example 1. These specific examples taught by Baracchini et al include the presently claimed phosphorothioate linkages, 2'-O-methoxyethyl sugars, 5-methylcytosine and chimeric oligonucleotides. Tables 1-4 show the successful design and use of modified oligonucleotides in cells in culture. Table 1 exemplifies the successful practice of general antisense design taught at columns 8-10. Column 4 teaches various carriers for antisense delivery. Baracchini *et al.* also teaches at column 8 that antisense oligonucleotides are preferably 8 to 30 nucleotides and that it is more preferable to make



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antisense oligonucleotides that are 12 to 25 nucleotides in length. Baracchini is considered to comprise a detailed blueprint for how to make and use inhibitory antisense oligos to target any known gene.

The teachings of Bennett *et al.* are considered to parallel those of Baracchini *et al.* Bennett *et al.* teaches general antisense targeting guidelines at columns 3-4. Bennett *et al.* also teaches the coding region of a desired target. Bennett teaches, in column 5, for example, that antisense compounds are commonly used as research reagents and diagnostics. Column 5 indicates that antisense oligonucleotides 8-30 nucleotides in length are particularly preferred. Columns 6-7 teach that preferred antisense oligonucleotides contain modified internucleoside linkages including phosphorothioate linkages, among others. Columns 7-8 teach that preferred antisense oligonucleotides comprise modified sugar moieties including 2'-O-methoxyethyl. Bennett *et al.* also teach one of ordinary skill to modify nucleobases in antisense oligonucleotides, including the teaching of 5-methylcytosine (col. 8-9), and also to use chimeric antisense oligonucleotides (col. 9-10). Bennett *et al.* teach that the above modifications are known in the art to provide beneficial attributes to antisense oligonucleotides such as increased hybridization and nuclease protection, for example. Columns 10-24 teach numerous "carriers" for antisense oligonucleotides. Table 1 teaches the successful targeting of those regions taught in columns 3-4 with chimeric phosphorothioate oligonucleotides having 2'-MOE (a 2'-O-methoxyethyl modification). Thus, Bennett *et al.* is also considered to comprise a detailed blueprint for how to make and use inhibitory antisense oligos to target any known gene.

It would have been obvious to one of ordinary skill in the art to make antisense sequences to target the cDNA sequence of human collapsin response mediator protein 2

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as taught by Aguera et al. for inhibition of the instant human collapsin response mediator protein 2 of applicant's instant SEQ ID NO: 3 taught by Zhou. Furthermore, it would have been obvious to one of ordinary skill in the art to incorporate modifications as taught by Baracchini et al. into said antisense compounds.

One would have been motivated to create such compounds because Aguera et al. expressly teach antisense inhibition of the coding portion of applicants' instant human collapsin response mediator protein 2 target of SEQ ID NO: 3 in claiming a treatment for myelin disorders, and further, because Zhou et al. teaches the remainder of said target. One would have been motivated to modify said antisense compounds as taught by Baracchini *et al.* and Bennett *et al.*, because both teach that such modifications increase an antisense compound's cellular uptake, target affinity and resistance to degradation. Finally, one would have a reasonable expectation of success given that Taylor teaches that with software analysis and high affinity oligos, one needs to screen only 3-6 oligos to find one that inhibits its target 66-95%, and since Baracchini *et al.* and Bennett *et al.* both teach making modified antisense compounds targeted to distinct regions of a target gene, the steps of which are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz, Ph.D. whose telephone number is 571-272-0763. The examiner can normally be reached on 8:00-4:30 M-F. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

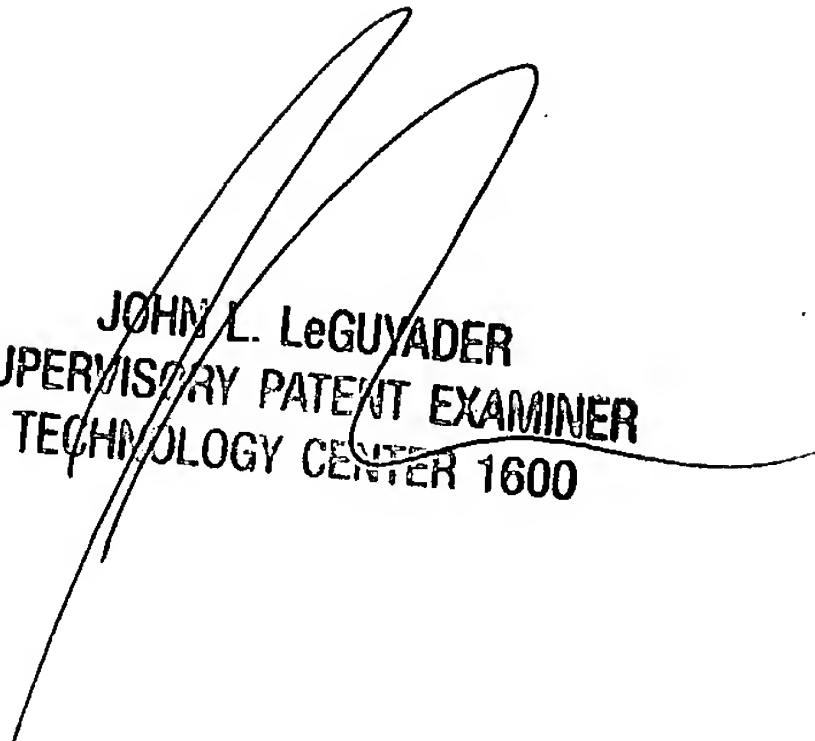
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